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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,770	12/29/2000	Kuber T. Sampath	00960-520PRO	7664

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EXAMINER	
LI, RUIXIANG	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,770	SAMPATH ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-38* is/are pending in the application.

4a) Of the above claim(s) *28-30,32 and 35-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-27,31,33,34 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 June 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1201* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicants' election with traverse of Group I, claims 20-27, 31, 33 (in part), 34 (in part), and 38 (in part), on September 22, 2003 is acknowledged. The traverse is on the ground that there will not be any undue burden on the Examiner to search the pending claims which all recite uses of morphogens. This has been fully considered but is not deemed to be persuasive while each group recites morphogens, the three invention groups are drawn to completely different methods each using different compositions, having completely different steps and biological outcomes. Invention Group I requires activation of an intracellular pathway (by a morphogen) that induces intracellular formation of a Smad complex; Invention Group II requires inhibiting TGF-β (by a morphogen) from promoting formation of scar tissue via fibrosis; whereas invention Group III is drawn to method for inhibiting TGF-β mediated fibrosis of tissue. Each method is unique and not required another. Thus, the methods are exclusive, which are not interchangeable and which require non-cohesive searches and considerations.

The Examiner has also acknowledged in Paper No. 13 Applicants' election in Paper No. 12 of the following species: (a) OP-1; and (b) Smad 1.

The requirement is still deemed proper and is therefore made FINAL.

2. Applicants' amendment filed in Paper No. 12 has been entered in full. Claims 1-19 have been canceled. Claims 20-38 are pending. Claims 20-27, 31, 33 (in part), 34 (in part), and 38 (in part) are under consideration. All other claims are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention

Priority

3. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §119(e) to U.S. provisional applications, 60/069,931 and 60/110,498.

Drawings

4. The drawings filed on 6/16/2000 are accepted the Examiner.

Information Disclosure Statement

5. The Information Disclosure Statement submitted on December 26, 2001 has been received by the Office. The references listed in PTO-1449 form have been fully considered by the Examiner.

Sequence Compliance

6. This application contains sequence disclosures that are encompassed by the definitions for amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821

through 1.825 because not all the amino acid sequences present in the specification (see, e.g., line 23 of page 1) have been identified with a SEQ ID NO (also see the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures). Furthermore, claim 38 recites "the C-terminal seven cysteine domain of human OP-1", which has not been identified with a SEQ ID NO.

All the amino acid sequences appearing in the specification and claims must be identified by a sequence identifier in accordance with 37 C.F.R. 1.821(d). Applicants must provide appropriate amendments to the specification or claims inserting the required identifiers. If the amendments are extensive then a substitute specification may be required.

Claim Rejections— Nonstatutory Obviousness-Type Double Patenting

7. Basis for nonstatutory double patenting:

7The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 20-24, 26, 27, 31, 33, 34, and 38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-

4, 19, and 20 of U.S. Patent No. 6,498,142 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons. U.S. Patent No. 6,498,142 B1 teaches a method of treatment for a mammal at risk of chronic renal failure, which comprises administering to said mammal a therapeutically effective amount of a morphogen, including OP-1. Treatment of cells with a morphogen (e.g., OP-1) necessarily causes specific binding of a morphogen to its transmembrane receptor and phosphorylation of a Smad protein, and induces translocation of Smad complex into the cell's nucleus, leading to expression of a phenotype-specific gene, since activation of an intracellular pathway that induces intracellular formation of a Smad complex is inherent to the morphogen (e.g., OP-1). In the instant application, the claims are drawn to a method for restoring cellular phenotype in a subject's cell affected by disease, damage or age, comprising administering to the subject an effective amount of a morphogen. Therefore, the patented claims are related to the instant claims as species to genus. A patented species renders its genus obvious and thus anticipates the genus.

9. Claims 20-25, 27, 31, 33, and 38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,531,445 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons. U.S. Patent No. 6,531,445 B1 teaches a method of inducing hepatic tissue growth in the liver tissue of a mammal and a method for repairing a damaged liver tissue. Both methods comprise providing a morphogen to the liver tissue. Treatment of cells with a

morphogen (e.g., human OP-1) necessarily causes specific binding of a morphogen to its transmembrane receptor and phosphorylation of a Smad protein, and induces translocation of Smad complex into the cell's nucleus, leading to expression of a phenotype-specific gene, since activation of an intracellular pathway that induces intracellular formation of a Smad complex is inherent to the morphogen. In the instant application, the claims are drawn to a method for restoring cellular phenotype in a subject's cell affected by disease, damage or age, comprising administering to the subject an effective amount of a morphogen. Therefore, the patented claims are related to the instant claims as species to genus. A patented species renders its genus obvious and thus anticipates the genus.

Claim Rejections—35 USC § 112, 1st paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 20-27, 31, 33, 34, and 38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the methods for restoring phenotypes of a cell taught by the instant specification and in the art, does not reasonably provide enablement for the full scope of the invention (see below). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claim 20 recites a method for restoring cellular phenotype in a subject's cell affected by disease, damage or age, comprising administering to the subject an effective amount of a morphogen to activate an intracellular pathway that induces intracellular formation of a Smad complex which induces expression of a phenotype-specific gene, thereby restoring the cellular phenotype in the subject's cell. Claims 21-27, 31, 33, 34, and 38 depend from claim 20. Thus, the claims are remarkably broad; they encompass any morphogens (either known or unknown at present time) , any intracellular pathways, any smad complexes, any types of cells and their phenotypes affected by any diseases, damages, or aging in any subjects. They encompass curing cancer cells, reversing process of aging and restoring youth, and revive a dead heart or a dead subject. Clearly an artisan would not be able to practice these methods in view of the state of the art and the relative skill of those in the art.

Accordingly, only the methods disclosed in the specification or taught in the art, not the full scope of the claimed invention, are enabled. Applicants are required

to amend the claims to limit the scope of the invention to those that are reasonably enabled in view of the teachings of the art and the instant specification.

Claim Rejections—35 USC § 112, 1st paragraph

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 20-27, 31, 33, and 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification discloses a number of morphogens, as listed in pages 1 and 2. However, claims 1 and 31 recite "morphogen", which includes members of the family of bone morphogenic proteins, which belong to the TGF-β superfamily (Kretzschmar et al., Genes & Development 11:984-995, 1997). The claims also read on the morphogens which have not been discovered yet. Claims 21-27 depend from claim 20, whereas claims 33 and 34 depend from claim 31.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed

product, or any combination thereof. In this case, the only factor present in the claims is the recitation of functional characteristics, "to activate an intracellular pathway that induces intracellular formation of a Smad complex which induces expression of a phenotype-specific gene". However, it is noted that mere recitation of a biological activity" does not provide sufficient description for the genus of morphogens. As the art teaches (e.g., Kretzschmar et al., Genes & Development 11:984-995, 1997) and as the specification acknowledged (page 2), while morphogens shares certain functional features, such as the ability to stimulate endochondral bone formation in an in vivo assay, or the ability to stimulate N-CAM or L1 isoform production in an NG108-15 neuronal cell culture, their structures do differ as judged by the disclosed morphogens. There are no common structural features among all the morphogens. Accordingly, in the absence of sufficient recitation of distinguishing both functional and structural characteristics, the specification does not provide adequate written description of the claimed genus of morphogens.

Therefore, only the morphogens disclosed in the specification, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections—35 USC § 112, 2nd paragraph

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 20-27, 31, 33, 34, and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it recites the term "Smad complex". It is unclear what the bounds and metes of the term are. Claims 21-27, 31, 33, 34, and 38 depend either directly or indirectly, from claim 20.

Claim 33 is indefinite also because it recites the term "soft tissue". Since neither the art nor the specification provides an unambiguous definition for the term, the claim is indefinite.

Claim Rejections—35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 20-24, 27, 31, 33, and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Rueger et al. (WO 94/03200, February 17, 1994).

Rueger et al. teach morphogen-induced nerve regeneration and repair. Specifically, Rueger et al. teach therapeutic treatment methods for maintaining neural pathways in a mammal, including enhancing survival of neurons (obviously a soft tissue cell) at risk of dying (due to chemical or mechanical trauma), inducing cellular repair of damaged neurons and neural pathways, and stimulating neurons to

maintain their differentiated phenotype (see, e.g., Abstract). The methods comprise providing a morphogen to said neurons at a concentration sufficient to enhance survival of said cells (e.g., claims 2-24). Rueger et al. further teach specific morphogens, including OP-1 and OP-2 (page 20, line 24). It is noted that activation of an intracellular pathway that induces intracellular formation of a Smad complex is inherent to the morphogen (e.g., OP-1). Treatment of cells with a morphogen (e.g., OP-1) necessarily causes specific binding of a morphogen to its transmembrane receptor and phosphorylation of a Smad protein, and induces translocation of Smad complex into the cell's nucleus, leading to expression of a phenotype-specific gene. Thus, the reference of Rueger et al. meets the limitations of claims 20-24, 27, 31, 33, and 38.

17. Claims 20-25, 27, 31, 33, and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuberasampath et al. (WO 94/06449, March 31, 1994).

Kuberasampath et al. teach morphogen-induced liver regeneration. Specifically, Rueger et al. teach therapeutic treatment methods for maintaining liver function in a mammal, including regenerating lost or damaged hepatic tissue, enhancing viability and integration of hepatic tissue and correcting liver function deficiencies (including enhancing diminished liver function due to tissue injury or disease)(see, e.g., Abstract). The methods comprise providing a therapeutically effective morphogen concentration to the hepatic cells that are obviously soft tissue cells (see, e.g., claims). Kuberasampath et al. further teach specific morphogens, including OP-1 and OP-2 (see, e.g., claims 41-44). It is noted that activation of an

intracellular pathway that induces intracellular formation of a Smad complex is inherent to the morphogen (e.g., OP-1). Treatment of cells with a morphogen (e.g., OP-1) necessarily causes specific binding of a morphogen to its transmembrane receptor and phosphorylation of a Smad protein, and induces translocation of Smad complex into the cell's nucleus, leading to expression of a phenotype-specific gene. Thus, the reference of Kuberasampath et al. meets the limitations of claims 20-25, 27, 31, 33, and 38.

Claim Objections—Minor Informalities

18. Claims 27, 33, 34, and 38 are objected to because of the following informalities: (i) claims 27 and 38 recites unelected subject matter (unelected species); (ii) claims 33, 34, and 38 depend from unelected claims.

Appropriate correction is required.

19. The prior art made of record in PTO-892 form and not relied upon is considered pertinent to applicant's disclosure.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (703) 306-0282. The examiner can normally be reached on Monday-Friday, 8:30 am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Ruixiang Li
Examiner
December 12, 2003